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Influence of β-glucan on nonspecific immunity and growth performance in weanling pigs

Abstract

Three experiments, using 344 pigs, were conducted to evaluate the influence of Î²-glucan (MacroGardâ„¢-S) on neutrophil and macrophage function, resistance to Streptococcus suis challenge, and growth performance in weanling pigs. Î²-glucan, when fed at inclusion rates of .05 and .1 %, did not influence neutrophil or macrophage function or increase overall growth performance. Similarly, .025% Î²-glucan did not alter neutrophil or macrophage bactericidal activity or production of superoxide anion. However, diets containing.025% Î²-glucan increased average daily gain, average daily feed intake, and pigs weights and decreased plasma haptoglobin levels on d 21. Unfortunately, pigs fed a diet containing .025% that exhibited increased growth performance were more likely to die after challenge with S. suis. These data suggest the existence of a complex interaction involving growth performance and resistance to S. suis in pigs fed .025% Î²-glucan. The interaction should be investigated further.; Swine Day, Manhattan, KS, November 17, 1994

Keywords

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INFLUENCE OF β-GLUCAN ON NONSPECIFIC IMMUNITY AND GROWTH PERFORMANCE IN WEANLING PIGS[1]

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Summary

Three experiments, using 344 pigs, were conducted to evaluate the influence of β-glucan (MacroGard™-S) on neutrophil and macrophage function, resistance to *Streptococcus suis* challenge, and growth performance in weanling pigs. β-glucan, when fed at inclusion rates of .05 and .1%, did not influence neutrophil or macrophage function or increase overall growth performance. Similarly, .025% β-glucan did not alter neutrophil or macrophage bactericidal activity or production of superoxide anion. However, diets containing .025% β-glucan increased average daily gain, average daily feed intake, and pigs weights and decreased plasma haptoglobin levels on d 21. Unfortunately, pigs fed a diet containing .025% that exhibited increased growth performance were more likely to die after challenge with *S. suis*. These data suggest the existence of a complex interaction involving growth performance and resistance to *S. suis* in pigs fed .025% β-glucan. The interaction should be investigated further.

(Key Words: Starter Pigs, β-glucan, Growth.)

Introduction

Increasing innate immunity in young pigs is one means of decreasing disease susceptibility and presumably increasing growth performance. Glucans from a variety of bacterial, yeast, and plant cell walls have been shown to stimulate both specific (vaccine adjuvants) and nonspecific immune responses. When one considers the mechanisms responsible for the positive results obtained from feeding β-glucan to weaned pigs, several possibilities exist. First, is the response evoked by eliciting specific immune reactions? If weaned pigs were vaccinated close to the time that β-glucan was administered in the feed, it is conceivable that immunity to specific vaccine immunogens could result. However, unless the animals were exposed to the particular vaccine pathogens during the nursery phase, it is difficult to imagine an increase in growth performance from the generation of specific immunity to vaccine antigens. Second, is the positive growth response evoked by enhancement of nonspecific immunity? Primary targets of β-glucan activity are phagocytic cells of the immune system, such as neutrophils and macrophages. It is conceivable that increasing phagocytic cell function could lower the innate pathogen load in young pigs and act

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much like a low-level antibiotic feed additive. Finally, because delayed-type hypersensitivity (DTH) is an immune response capable of being modulated, one could imagine a mechanism whereby feeding an immunomodulator in the nursery diet might abate soybean-induced DTH by enhancing tolerance to soybean proteins. We conducted three experiments feeding β-glucan to weaned pigs to address some of these possibilities. In Exp. 1, we evaluated the influence of diet (all milk protein vs soybean meal) and .1% β-glucan on growth performance and neutrophil function in weaned pigs. In Exp. 2, the influence of .1% β-glucan on growth performance was evaluated in weaned pigs in a large-scale on-farm trial. In Exp. 3, we evaluated the influence of .025 and .05% β-glucan on growth performance, neutrophil and macrophage function, acute phase protein production, and resistance to a *Streptococcus suis* infection in weaned pigs.

Procedures

Experiment 1: One hundred forty-four crossbred pigs were weaned at 3 wk of age and allotted by weight, gender, and ancestry to four treatment groups in a 2 × 2 factorial arrangement of nursery diet and β-glucan treatment. Pigs were housed in an environmentally controlled nursery with woven-wire flooring. Each pen contained a self-feeder and a nipple waterer to provide ad libitum access to feed and water. Six pigs were housed per pen (4 ft × 5 ft) with six replicate pens per treatment. From weaning to d 7 postweaning, all pigs were fed a common milk-protein-based diet (Table 1). On 7 d postweaning, 72 pigs were switched to a soybean-meal-based diet. The remaining pigs were fed a milk-protein-based diet that did not contain any soybean meal. Within dietary treatments, pigs were assigned to control or .1% β-glucan treatments. Pig weights and feed consumption were collected weekly postweaning to calculate average daily gain (ADG), average daily feed intake (ADFI), and feed efficiency (F/G).

Starting on d 7 postweaning, whole-blood samples were collected weekly from six pigs on each treatment for assessment of neutrophil function. Neutrophils were isolated and evaluated for generation of reactive oxygen intermediates, antibody-dependent cellular cytotoxicity, and bactericidal activity. In addition, a whole-blood flow cytometric assay for neutrophil oxidative burst was conducted. Superoxide anion production and bactericidal activity against *Streptococcus suis* were evaluated only in pigs on the milk-based diet.

Experiment 2: One hundred forty pigs were weaned at 14 d of age and assigned to control or .1% β-glucan diets. Pigs were housed in an environmentally controlled nursery with slotted-metal flooring on a commercial farm in northeast Kansas. Each pen contained a self-feeder and two nipple waterers to provide ad libitum access to feed and water. Six, seven, or nine pigs were housed per pen (4 ft × 6 ft) with nine replicate pens per treatment. Pigs were fed Phase I diets from weaning to d 14 postweaning and then switched to Phase II diets from d 14 to 28 postweaning (Table 1). Pigs were fed their respective control or β-glucan treatment for the entire 28-d study. Pig and feeder weights were collected weekly postweaning to calculate ADG, ADFI, and F/G.

Experiment 3: Sixty crossbred pigs were weaned at 3 weeks of age and allotted by weight, gender, and ancestry to three dietary treatment groups: 0, .025, and .05% β-glucan (Table 1). Pigs were housed in an environmentally controlled, isolation facility in polyethylene pens. Each pen contained a self-feeder and a nipple waterer to provide ad libitum access to feed and water. Four pigs were housed per pen with five replicate pens per treatment. Pig weights and feed consumption were collected weekly postweaning to calculate ADG, ADFI, and F/G.

On d 14 and 28, alveolar macrophages were collected from five pigs on each treatment by bronchoalveolar lavage. Macrophage functions evaluated included generation of superoxide anion production and bactericidal activity. Additionally, macrophage expression of the membrane antigen CD14, a receptor for lipopolysaccharide (LPS), was evaluated on d 14 and 28. On d 26, neutro-

phils were collected (five pigs/treatment) and assayed for superoxide anion production and bactericidal activity. At d 0, 7, 14, 21, 28, and 35 plasma was collected from two pigs per pen for analysis of the acute phase protein, haptoglobin.

After 4 wk on the experimental diets, all pigs were injected intravenously with 6.5×10^8 colony forming units of a log-phase culture of *S. suis*, serotype 2. Pigs were observed daily following challenge and the following clinical signs were recorded: dyspnea, depression, lameness, and CNS disorders. Scoring of clinical signs was 0 to 3 (normal to severe) for dyspnea, depression, and CNS disorders and 0 to 4 (normal to down) for lameness. A pooled clinical score was calculated for each pig. Rectal temperatures were monitored daily. All pigs were euthanitized by electrocution at 12 d after infection.

Data were analyzed according to the General Linear Models procedure of the Statistical Analysis System. Mortality data were analyzed by Fisher's Exact Test. Haptoglobin levels were analyzed using repeated measures analysis of variance with a Satterthwaite error correction for comparisons of treatments within day postweaning.

Results

Inclusion of β-glucan at .1% of the diet did not increase growth performance in nursery pigs (Table 2). Conversely, pigs fed the milk-based diet containing β-glucan had numerically decreased growth performance during the first 2 weeks on the diet. Pigs fed the soybean-meal-based diet had depressed growth performance in comparison to pigs fed the milk-based diet; however, adding .1% β-glucan to the diet did not abate this depression. Because β-glucan did not produce the expected increase in growth performance, a second experiment was conducted with a different lot of β-glucan. However, feeding .1% β-glucan-supplemented diets for 4 weeks to nursery pigs did not influence growth performance (Table 3).

Inclusion of β-glucan at rates less than .1% may be more effective in enhancing growth performance. Based on data that became available to us after the conclusion of the first two experiments, β-glucan inclusion rates of .025 and .05% were evaluated in Exp. 3. Average daily gain was increased in pigs fed a diet supplemented with .025% β-glucan for 4 wk (Table 4). This increased gain was the result of increased feed intake and resulted in approximately a 5 lb weight advantage after 4 wk on the diet. Numerically, ADG, ADFI, and pig weights were greater in pigs fed .05% β-glucan than pigs fed the control diet. However, after *S. suis* challenge on d 28 postweaning, ADG was threefold less in pigs fed β-glucan than in pigs fed the control diet.

In general, oral β-glucan had no consistent effects on peripheral blood neutrophil generation of reactive oxygen intermediates, antibody-dependent cellular cytotoxicity, or bactericidal activity. Macrophage and neutrophil production of superoxide anion and bactericidal activity against *S. aureus* were not influenced by diets containing .025 and .05% β-glucan. Similarly, macrophage expression of the LPS receptor, CD14, was not influenced by inclusion of β-glucan in diets.

An interaction occurred between dietary treatments and day postweaning on plasma haptoglobin concentration (Figure 1). The interaction resulted in lower concentrations of haptoglobin produced on d 14 and 21 postweaning in the pigs fed .025% β-glucan.

Inoculation of pigs with 6.5×10^8 colony forming units of *S. suis*, caused a rapid expression of streptococcal disease in all pigs. However, pigs that displayed the best growth performance, i.e., pigs fed the .025% β-glucan diet, were more susceptible to the streptococcal infection than pigs fed the control diet (Figure 2). This finding was evident in rectal temperatures and clinical signs of the disease and was most clearly demonstrated by the 50% mortality rate in pigs fed .025% β-glucan.

Discussion

Three points are clear from these β-glucan experiments. First, with three different dietary regimens, we observed no benefit of supplementing nursery-pig diets with .1% β-glucan. Second, nursery-pig diets supplemented with .025% β-glucan increased growth performance. Third, pigs that exhibited increased growth performance caused by a diet containing .025% β-glucan were more likely to die after challenge with *S. suis*.

Our data suggest that a discrete dose relationship exists between dietary levels of β-glucan, growth performance, and resistance to streptococcal disease. In our first experiment using .1% β-glucan, growth performance was decreased during the first 2 wk of the study; however, this finding was not observed in the second trial using .1% β-glucan. It is known that β-glucan can augment interleukin-1 secretion in macrophages that are activated by LPS. If immune activation does limit growth performance, perhaps the data from Exp. 1 reflect this concept. However, why was the growth depression observed only during the first 14 d in Exp. 1 and not in Exp. 2? Because of disease problems (*S. suis*), pigs in Exp 1. were water medicated at about wk 2 of the trial. The water medication may have reduced the pathogen load and, thus, the degree of immune activation and may have decreased any interleukin-1 priming-effect of β-glucan on activated immune cells. Although β-glucan has been shown to augment interleukin-1 secretion in activated macrophages, it is also known that β-glucan can preferentially cause the secretion of a competitive inhibitor of interleukin-1. If feeding β-glucan alters the balance of interleukin-1 and the competitive inhibitor of interleukin-1 such that the inhibitor is preferentially secreted, then one would expect less activation of the immune system during the feeding period, which might result in increased growth performance. This is further supported by the data indicating decreased production of acute phase proteins in the pigs fed .025% β-glucan. Interleukin-1 and other cytokines are critical for the production of the acute phase proteins of the immune response. Thus, the decreased level of acute phase proteins could indicate suppression of cytokine production. However, because interleukin-1 is a pivotal cytokine in an animals' resistance to bacterial disease, one would expect an individual with lower interleukin-1 capabilities to be at a disadvantage during a bacterial infection. Indeed, this scenario may explain our findings of increased growth performance prior to challenge with *S. suis* and increased disease susceptibility after *S. suis* challenge in pigs supplemented with .025% β-glucan.

In conclusion, our findings suggest that supplementing nursery-pig diets with .025% β-glucan increased growth performance. However, because this treatment also increased disease susceptibility to *S. suis*, our data suggest that a complex interaction exists between growth performance and disease susceptibility in pigs fed β-glucan. The implications of this last finding are extremely important, and we recommend that further studies be conducted to confirm or refute the involvement of β-glucan in the interaction of growth performance and disease susceptibility.

Table 1. Diet Composition[a]

Item	Exp. 1 Phase 1	Exp. 1 Milk	Exp. 1 Soy	Exp. 2 Phase 1 and Exp. 3	Exp. 2 Phase 2
Corn	42.13	52.14	42.31	37.45	56.44
Dried whey	25.00	20.00	10.00	25.00	10.00
Soybean meal (48.5% CP)	--	--	38.47	19.14	23.54
Dried skim milk	10.00	5.00	--	--	--
Casein	4.82	4.32	--	--	--
Spray-dried porcine plasma	7.50	7.50	--	7.50	--
Soybean oil	5.00	5.00	5.00	5.00	3.00
Spray-dried blood meal	1.75	1.75	--	1.75	2.50
Monocalcium phosphate (21% P)	1.60	1.90	1.69	1.74	1.93
Antibiotic[b]	1.00	1.00	1.00	1.00	1.00
Limestone	.53	.66	.78	.63	.82
Vitamin premix	.25	.25	.25	.25	.25
Trace mineral premix	.15	.15	.15	.15	.15
DL-methionine	.10	.04	.02	.173	.90
Copper sulfate	.075	.075	.075	.075	.075
L-lysine HCl	.10	.10	--	.10	.10
Cornstarch[c]	--	.10	.10	.05	.10
Total	100	100	100	100	100

[a]Diets in Exp. 1, Exp. 2 Phase 1 (d 0 to 14 postweaning) and Exp. 3 were formulated to contain 1.6% lysine and .46% methionine. Diets in Exp. 2 Phase 2 (d 14 to 28) were formulated to contain 1.25% lysine and .35% methionine. All diets were formulated to contain .9% calcium and .8% phosphorus. Exp. 1 Phase 1 was fed from d 0 to 7 postweaning, and soy or milk diets were fed from d 7 to 35 postweaning.
[b]To provide 50 g/ton carbadox.
[c]β-glucan was substituted for cornstarch to provide .1% β-glucan in Exp. 1 and 2 and .025% and .05% β-glucan in Exp. 3.

Table 2. Effects of Diet and β-Glucan on Growth Performance of Weanling Pigs (Exp. 1)[a]

Item	Milk Control	Milk .1% β-glucan	Soybean meal Control	Soybean meal .1% β-glucan	CV
d 7 to 14 postweaning					
ADG, lb[b]	.76	.63	.40	.40	15.3
ADFI, lb[b,c]	.92	.73	.73	.65	10.1
F/G[b]	1.13	1.27	1.97	1.74	19.1
d 7 to 35 postweaning					
ADG, lb[b]	1.04	1.02	.75	.75	10.1
ADFI, lb	1.39	1.29	1.32	1.30	7.2
F/G[b]	1.32	1.29	1.76	1.76	11.2
Pig weight, lb					
d 35[b]	44.9	43.7	36.3	36.7	6.3

[a]A total of 144 pigs was used (initially 11.1 lb and 21 d of age), six pigs/pen, six pens/treatment. All pigs were fed a common diet (milk) from d 0 to 7 postweaning. Dietary treatments were fed from d 7 to 35 postweaning. Values are means of six pens adjusted using average weight on d 7 as a covariate.
[b]Diet main effect ($P < .01$).
[c]Glucan main effect ($P < .01$).

Table 3. Effects of β-Glucan on Growth Performance of Weanling Pigs (Exp. 2)[a]

Item	Control	.1% β-Glucan	CV
d 0 to 14 postweaning			
ADG, lb	.51	.53	12.5
ADFI, lb	.60	.59	11.9
F/G	1.19	1.15	6.8
d 14 to 28 postweaning			
ADG, lb	.76	.76	10.3
ADFI, lb	1.29	1.23	7.1
F/G	1.73	1.63	7.4
d 0 to 28 postweaning			
ADG, lb	.63	.64	10.6
ADFI, lb	.94	.91	8.1
F/G	1.51	1.44	6.0

[a]A total of 140 pigs was used (initially 8.7 lb and 14 d of age) with six, seven, or nine pigs/pen and nine pens/treatment. Pigs were fed Phase I diets from d 0 to 14 postweaning and then switched within treatment to Phase II diets from d 14 to 28 postweaning. No treatment effects.

Table 4. Effects of β-Glucan on Growth Performance of Weanling Pigs (Exp. 3)[a]

Item	Control	.025% β-Glucan	.05% β-Glucan	CV
d 0 to 14 postweaning				
ADG, lb	.71[b]	.83[c]	.73[b]	12.0
ADFI, lb	.68[b]	.82[c]	.70[b]	11.4
F/G	.97	.99	.97	2.2
d 14 to 28 postweaning				
ADG, lb	1.11[b]	1.34[c]	1.23[b]	8.4
ADFI, lb	1.15[b]	1.41[c]	1.28[b]	13.7
F/G	1.20	1.22	1.24	10.1
d 0 to 28 postweaning				
ADG, lb	.91[b]	1.09[c]	.98[b]	11.9
ADFI, lb	.95[b]	1.17[c]	1.06[b]	13.2
F/G	1.06	1.08	1.08	5.9
d 28 to 35 postweaning[d]				
ADG, lb	.31	.08	.02	389
Pig weight, lb				
d 14 postweaning	20.8[e]	22.4[f]	20.9[e]	6.0
d 28 postweaning	36.3[b]	41.1[c]	38.1[b]	6.4

[a]Total of 60 pigs was used (initially 10.8 lb and 18 d of age) with four pigs/pen on d 0 to 14, three pigs/pen on d 15 to 28, and two pigs per/pen on d 29 to 35. There were five pens/treatment.
[b,c]Means lacking a common superscript differ ($P < .05$).
[d]ADG after *S. suis* challenge.
[e,f]Means lacking a common superscript differ ($P < .10$).

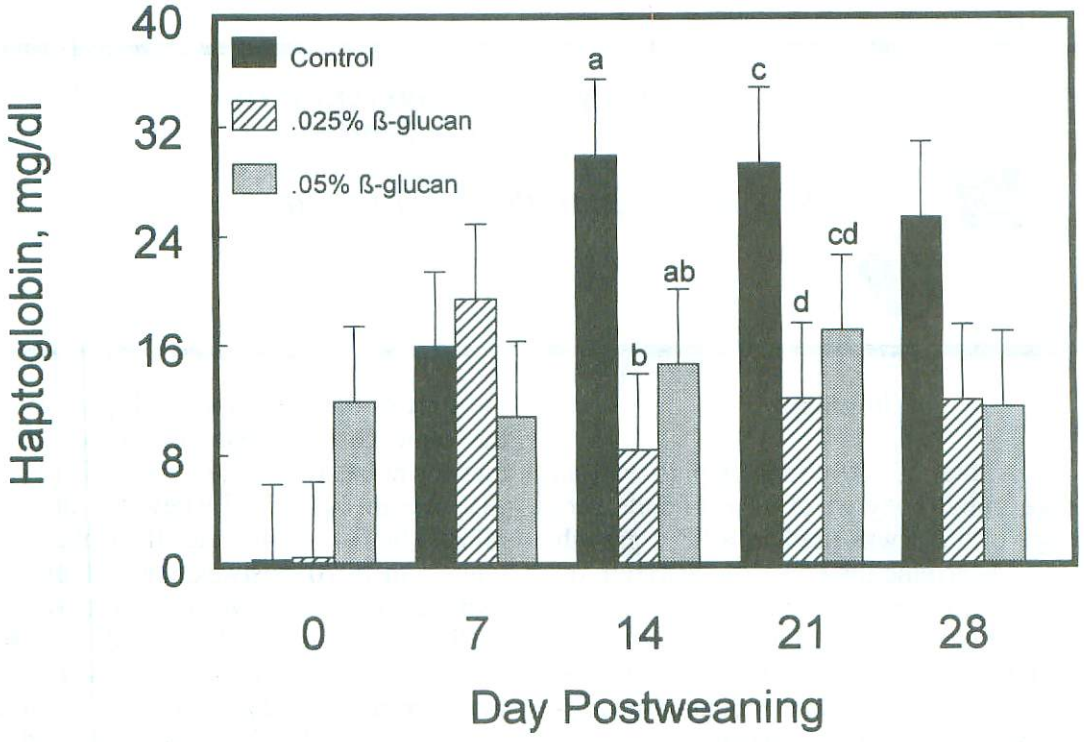

Figure 1. Plasma Haptoglobin Concentrations in Pigs Fed β-Glucan and Challenged with *S. suis*. (Pigs were fed diets supplemented with .025 and .05% β-glucan for 4 wk and inoculated intravenously with *S. suis* serotype 2 (6.5×10^8 CFU) at d 28. Values are means ± SEM, n=10. Means within day lacking a common superscript differ, $^{a,b}P < .07$ and $^{c,d}P < .14$.)

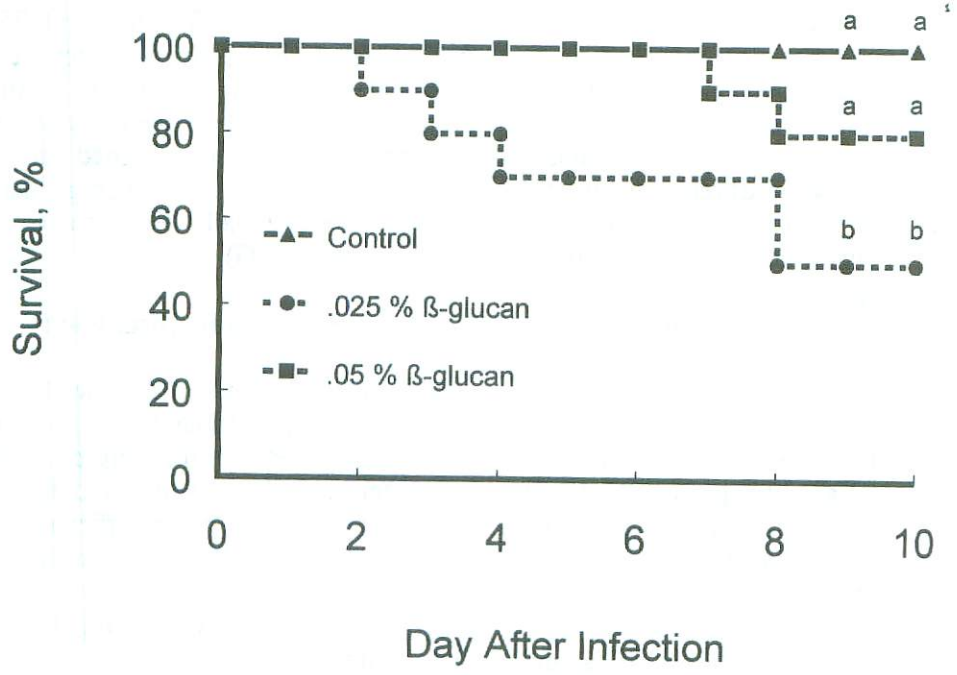

Figure 2. Survival Rates of Pigs after *S. suis* Challenge. (Pigs were fed diets supplemented with .025 and .05% β-glucan for 4 wk and inoculated intravenously with *S. suis* serotype 2 (6.5×10^8 CFU) at d 28. Ten pigs were on each diet. Values within day lacking a common superscript differ, P < .04.)